REMARKS

Claims 1-13 and 17-31 and 33-34 are active. Claim 32 has been withdrawn from consideration. Claims 1 and 17 have been further clarified and limited, for example, the B group is not isoleucine (I). Support for this amendment is found in the original claims. Claim 33 finds support in the specification on page 5, lines 21-22 and Claim 34 at page 3, line 23-page 4, lines 1-3. Other minor editorial revisions have also been made to some claims. Accordingly, the Applicants do not believe that any new matter has been added.

The Applicants thank Examiner Teller for the courteous and helpful interview of January 19, 2005. Amendments which would help clarify and simplify the claim language were discussed as possible ways to address the enablement rejection, as well as the art rejection. It was suggested that Claim 1 be simplified, for instance, to be more like Claim 2, except that the center section of the formula of Claim 1 might be retained. Limitation of the B group in Claim 1 to exclude isoleucine was discussed. The Applicants believe that the amendments above accord with these suggestions. Isoleucine has been dropped from group B, the Z residues explicitly defined as serine (S), and the residues in the center section of the molecule clarified as: $(X_aB)_n(X_bB)_nX_cBX_d$. The terms "e" and "f" have been retained, but merely refer to peptides where the first two amino acid residues are both absent (when e and f = 0), or are both present (when e and f = 1). Favorable consideration is now respectfully requested.

Rejection—35 U.S.C.§112, first paragraph

Claims 1-13, 17-19, 21-22 and 28-31 were rejected under 35 U.S.C. 112, first paragraph, as lacking adequate enablement for an SP-C analog having formula (I) (SEQ ID NO: 1). The concern was that the claims were so broad as not to be enabled. Claim 1 is now directed to an analog which has up to 22 amino acid residues, comprises completely defined

amino acid sequences at both the N and C ends, and where the center section is defined by a stretch of a limited number of B and X residues, which themselves are limited to particular groups of amino acid residues. As discussed below, these center section residues which incorporate "B" provide analogs with superior functional properties (e.g., by virtue of B having a strong charge or providing steric hindrance to self-aggregation). The claimed peptide analogs all share multiple common structural features at each end as well as in their center sections. Moreover, the specification, clearly describes methods for making these peptides as well as a description of how to use them by disclosing their functional properties (see Examples 1-7 and Figs. 1-3) by showing these properties both *in vitro* and *in vivo*.

The Official Action indicated that there was insufficient guidance in the application for functional SP-C analogs of SEQ ID NO: 1. One important technical problem underlying the invention was to provide synthetic peptide analogs of the natural SP-C peptide, which, unlike known synthetic SP-C analogues:

- *are able to fold like the native peptide and so to interact properly with the surfactant lipids* (pg. 3, lines 23-28 to page 4, lines 1-2);
- *do not give rise to self-oligomerization* (pg. 4, lines 10-12).

The invention solves this technical problem by providing synthetic peptide analogs of SP-C wherein:

- *the Val residues* (in the 'center portion' of the SP-C native form) *have been substituted with outer neutral and hydrophobic residues* (pg. 5, lines 14-15).
- some of the neutral amino acid (in the 'center portion' of the SP-C native form) have been replaced with bulky or polar residues (pg. 5, lines 16-17).
- said peptides *showing particularly favorable properties for surface tension reduction* (pg. 5, lines 18-19).

In particular the residue L *strongly favors α-helical conformation* (pg. 4, lines 4-6) and the residues K, W, F, Y, and ornithine, *by virtue of the positive charges conferred by the polar residues or the steric hindrance conferred by the bulky substituents allow the claimed peptide analogs to avoid self-oligomerization* (pg. 5, lines 19-22). Accordingly, in view of the above arguments, as well as taking into account the scope of the claims and the amount of guidance provided by the specification, the Applicants respectfully request that this rejection be withdrawn.

Rejections—35 U.S.C. §102 and §103

Claims 1 and 7 were rejected under 35 U.S.C. §102 and §103 as being anticipated or unpatentable over Benson et al., WO 91/18015. The Applicants submit that these rejections are moot in view of the amended claim language. In present Claim 1, the meanings of B have been restricted to K, W, F, Y, and ornithine, *m* has been deleted, *n* is 0 or 1, and the central portion $(X_aB)_n(X_bB)_nX_cBX_d$ is a sequence having a maximum of 22 amino acids:

$$(X_aB)_n(X_bB)_nX_cBX_d$$

where B is: K,W, F, Y, and Ornithine (i.e., charged or sterically bulky amino acids); and

X is: I, L, and Nle (norleucine).

However, the polypeptide of Benson (WO 91/18015) has the central region:

Leu-Leu-Ile-Z-Z-Z-Z-Z-Z-Leu-Ile-Z-Z-Z-Ile-Z

wherein Z is V (Val) or I (Ile). This polypeptide does not have the charged residues like lysine (K) or sterically bulky residues like phenylalanine (F).

When Benson's peptides carry Z = Ile, Benson's peptides they fail to anticipate the present claims, since they do not contain any of the bulky or sterically hindering substituents specified in B (K, W, F, Y, and ornithine). Also, when Benson's peptides include Val, they

do not conform to the "X" subsituent required by the present claims. Accordingly, the Applicants respectfully request that this rejection now be withdrawn.

CONCLUSION

The Applicants respectfully submit that this application is now in condition for allowance. Early notification to that effect is respectfully requested.

Respectfully submitted,

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